REVIEW

Helicobacter pylori infection in Canadian and related Arctic Aboriginal populations

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KJ Goodman, K Jacobson, S Veldhuyzen van Zanten. *Helicobacter pylori* infection in Canadian and related Arctic Aboriginal populations. Can J Gastroenterol 2008;22(3): 289-295.

In 2006, the Canadian Helicobacter Study Group identified Aboriginal communities among Canadian population groups most at risk of *Helicobacter pylori*-associated disease. The objective of this systematic review was to summarize what is known about the *H pylori*-associated disease burden in Canadian and related Arctic Aboriginal populations to identify gaps in knowledge. Six health literature databases were systematically searched to identify reports on *H pylori* prevalence in Canadian population groups, or any topic related to *H pylori* in Canadian Aboriginals, Alaska Natives or Aboriginals of other Arctic regions. Identified reports were organized by subtopic and summarized in narrative form. Key data from studies of *H pylori* prevalence in defined populations were summarized in tabular form. A few Arctic Aboriginal communities were represented in the literature: two Canadian Inuit; one Canadian First Nation; two Greenland Inuit; one Russian Chutkotka Native; and several Alaska Native studies. These studies uniformly showed elevated *H pylori* prevalence; a few studies also showed elevated occurrence of *H pylori*-related diseases and high rates of treatment failure. Based on the evidence, it would be warranted for clinicians to relax the criteria for investigating *H pylori* and related diseases in patients from Arctic Aboriginal communities, and to pursue post-therapy confirmation of eradication. Additional community-based research is needed to develop public health policies for reducing *H pylori*-associated health risks in such communities.

Key Words: *Arctic regions;* Helicobacter pylori*; Inuits; North American Indians; Prevalence; Systematic review*

L'infection à Helicobacter pylori au sein de la population canadienne et de populations autochtones arctiques liées

En 2006, le groupe d'étude canadien de *Helicobacter pylori* a repéré des communautés autochtones au sein de groupes canadiens de populations plus vulnérables aux maladies associées à *H pylori*. La présente analyse systématique visait à résumer ce que l'on sait du fardeau des maladies associées à *H pylori* au sein de la population canadienne et de populations autochtones arctiques liées afin de dépister les lacunes du savoir. Les auteurs ont procédé à des recherches systématiques dans six bases de données de publications en santé afin de trouver des rapports sur la prévalence de *H pylori* au sein des groupes canadiens de populations ou sur tout sujet relié à *H pylori* chez les autochtones canadiens, les autochtones de l'Alaska ou ceux des autres régions arctiques. Ils ont classé les rapports obtenus en sous-sujets et les ont résumé sous forme narrative. Ils ont résumé les principales données des études sur la prévalence de *H pylori* dans des populations définies, sous forme de tableaux. Quelques communautés autochtones arctiques étaient représentées dans les publications : deux études sur les Inuits du Canada, une sur les autochtones des Premières nations du Canada, deux sur les Inuits du Groënland, une sur les autochtones chutkotka de la Russie et plusieurs sur les autochtones de l'Alaska. Ces études ont toutes révélé une prévalence élevée de *H pylori*, et quelques-unes, une occurrence élevée de maladies reliées à *H pylori* et de forts taux d'échec du traitement. D'après ces données probantes, il serait justifié que les cliniciens relâchent les critères d'exploration de *H pylori* et des maladies connexes chez les patients des communautés autochtones arctiques et qu'ils confirment l'éradication après le traitement. D'autres recherches en milieu communautaire pour mettre au point des politiques de santé publique visant à réduire les risques de santé reliés à *H pylori* s'imposent au sein des ces communautés.

Chronic *Helicobacter pylori* infection is estimated to affect one-half or more of the world's population (1). In 2005, Barry Marshall and Robin Warren were awarded the Nobel Prize for identifying this Gram-negative bacterium in 1982, an achievement that led researchers to discover in subsequent years its role in chronic gastritis, peptic ulcer disease and gastric cancer (2). The recognition of this achievement reflects the global public health importance of this infectious cause of widespread digestive diseases. In particular, gastric cancer is the second most frequent cancer worldwide, for both incidence and mortality (3). Although its frequency declined dramatically during the 20th century in affluent populations, rates remain high in many less affluent parts of the world. In settings where socioeconomic development favours control of infectious disease transmission, knowledge of *H pylori* has improved management of peptic ulcer disease and other *H pylori*-related conditions. However, this bacterium, now believed to have a long history as an unsuspected cause of chronic disease, has proved difficult to treat in high-risk communities. While the transmission of *H pylori* infection appears to have diminished in settings with modern sanitation infrastructures, the same is not true in settings where infectious diseases are easily spread. Epidemiological evidence shows that chronic *H pylori* infection is most frequently acquired in childhood, and is associated with household crowding and having infected family members (1). The low prevalence of *H pylori* infection in selected populations of children born in Canada, as reported by Jacobson (4) (Table 1), suggests that current levels of *H pylori* transmission are low in major Canadian urban centres. However, there are still large numbers of Canadians

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Received for publication August 17, 2007. Accepted November 13, 2007

TABLE 1
***Helicobacter pylori* prevalence in populations of interest**

Reference	Location	Population characteristics	Mean age, years	n	HP+, %
Canadian multiethnic populations					
Drumm et al, 1990 (75)	Hospital for Sick Children (Toronto, Ontario)	Upper gastrointestinal endoscopy patients	13	93	26
		Parents of patients	42	67	49
		Unrelated persons	16	37	14
Veldhuyzen van Zanten et al, 1994 (22)	Nova Scotia	Random sample, provincial medical insurance registry	18–72	316	38
			20–29	28	21
			30–39	68	28
			40–49	79	39
			50–59	51	41
			60–69	72	47
			70–79	16	50
Perez-Perez et al, 1997 (24)	Manitoba	Healthy persons	>20	469	35
			35–65	265	46
Hodgins et al, 1998 (35)	Southern Quebec	Cord blood samples, consecutive births	maternal age range	99	10
Thomson et al, 2003 (25)	49 family physician practices in 6 provinces	Patients with uninvestigated dyspepsia	18–86	1013	30
Armstrong et al, 2005 (76)	46 family physician practices across Canada	Patients with uninvestigated heartburn-dominant dyspepsia	18–83	390	31
Jacobson, 2005 (4)	4 academic centres	Pediatric endoscopy patients	5–18	246	5
Canadian Aboriginal populations					
Hodgins et al, 1998 (35)	Nunavik, northern Quebec	Cord blood samples, consecutive Inuit births	maternal age range	100	27
Bernstein et al, 1999 (33)	Northern Manitoba	Wasagamack Cree adults	adult ages	306	95
Sinha et al, 2002 (34)		Wasagamack Cree children	0–12	163	56
			7–9	23	70
			0–1	22	20
McKeown et al, 1999 (32)	Chesterfield Inlet and Repulse Bay, Nunavut	Inuit communities	all ages	256	51
			0–15	28	32
Northern Aboriginal populations outside of Canada					
Fenger and Gudmand-Hoyer, 1997 (28)	Greenland	Dyspeptic adults	no data	56	61
Reshetnikov et al, 1998 (30)	Russia, coastal Arctic region	Chutkotka Native adult males	32	34	77
Milman et al, 2003 (26)	Nuuk, Greenland	Population survey participants	22–76	71	47
Johansen et al, 2004 (29)	Greenland	Dyspeptic adults	≥18	100	77
Koch et al, 2005 (27)	Sisimiut, Greenland	Population-based sample	15–87	685	58
Zhu et al, 2006 (31)	Norton Sound (Alaska, USA)	Rural village residents	all ages	610	80
			0–24	–	72

HP+ Helicobacter pylori-*positive*

who harbour *H pylori* infections acquired in earlier eras or other parts of the globe, and some Canadian settings have suboptimal living conditions where endemic *H pylori* transmission appears to continue. In a 2006 workshop attended by the authors, the Canadian Helicobacter Study Group identified three groups of Canadians as the most at risk of *H pylori*-associated disease: the elderly, immigrants and Aboriginal populations. The objective of the present review was to summarize the evidence regarding the disease burden that is attributable to *H pylori* infection in Canadian and related Arctic Aboriginal populations, to assess what is known and what research is needed to fill gaps in knowledge.

BACKGROUND

Aboriginal people of Canada and other Arctic regions

Canadian census data from 2001 indicate that approximately 1.3 million Canadians reported having some Aboriginal ancestry, and more than 970,000 people (3.3% of all Canadians) identified themselves as Aboriginal. Among these people, 62% identified themselves as North American Indians (First Nations), 30% as Métis, 5% as Inuit and 3% identified with either more than one or none of these categories (5). Within Canada, Ontario (the most populous province) had the highest number of Aboriginals (n=188,315), followed by British Columbia (n=170,025) and the prairie provinces: Alberta (n=156,220), Manitoba (n=150,040) and Saskatchewan (n=130,190). The proportion of Aboriginals among the total population for these five provinces, respectively, were 2%, 4%, 5%, 14% and 14%. Aboriginals made up a higher population proportion in the northern territories: 85% in Nunavut, 51% in the Northwest Territories and 23% in the Yukon (5).

Canadian First Nations communities belong primarily to the following linguistic and cultural families: Algonquian – notably Cree and Ojibway – across the Atlantic provinces,

Ontario, Quebec and the Prairies; Iroquoian in Ontario and Quebec; Siouan (mainly Dakota) and Athabascan (mainly Chipewayan) in the Prairies; Athabascan in the northern territories; and various Northwest Coast Culture groups in British Columbia (6). Census 2001 data showed Canada's 608,850 North American Indians concentrated in five provinces: 22% in Ontario, 19% in British Columbia, 15% in Manitoba, 14% in Alberta and 14% in Saskatchewan; they made up 29% of the population of the Northwest Territories, 20% in the Yukon, 9% in Saskatchewan and 8% in Manitoba. Less than one-half lived on a reserve, with the largest numbers (in descending order) in Winnipeg, Vancouver, Edmonton, Toronto and Saskatoon (5).

The Métis, originally descended from Indian and European unions, gradually established their own collective identity along with a network of kinship connections and settlements that emerged from the fur trade along waterways of Ontario and northwestern Canada (7). Of the 292,310 Métis identified in the 2001 census, 23% lived in Alberta, 19% in Manitoba, and 17% in Ontario. Sixty-eight per cent lived in urban areas, with the largest numbers in Winnipeg, Edmonton, Vancouver, Calgary and Saskatoon (5).

The Inuit are descendants of the Sivullirmiut, believed to have migrated approximately 5000 years ago from the Bering land bridge eastward across the circumpolar region, establishing small communities across Alaska (USA), Canada and Greenland. Formerly called Eskimo, Inuit peoples include the Yupik and Inupiat of Alaska and the Russian Chutkotka region (Chukchi Peninsula), and the Inuit of Canada and Greenland. A defining characteristic of Inuit culture from Alaska to Greenland is the centuries-old technology for using the winter sea ice environment to hunt marine mammals (8). Of the 45,070 Inuit people identified in the 2001 Canadian census, one-half lived in the northeastern territory of Nunavut and 21% lived in Quebec, making up 85% of Nunavut's population, and less than 1% of Quebec's population (5). Most Canadian Inuit communities are coastal, and accessible only by air; the four major Inuit settlement regions include 23,000 people in 26 communities in Nunavut, 8000 in 14 communities in Nunavik (northern Quebec), 4500 in seven communities in Nunatsiavut (northern Labrador) and 5000 in six communities in Inuvialuit (western Arctic, Northwest Territories) (8,9).

The major ethnic group in Greenland is the Kalaallit Inuit, who made up 89% of Greenland's 2007 population of 56,648 (10). Aboriginal groups made up 16% of Alaska's population (estimated at 670,000 in 2006) (11). In addition to the Inuit, other Aboriginal groups in Alaska include the Aleut and Alutiiq peoples, who separated from early Inuit ancestors approximately 4000 years ago and were heavily influenced by Russian culture, as well as Athabascan and Northwest Coast Culture Native American groups (12). Among the Inuit, migration from Alaska to Canada continued in recent generations (13), and migration from Canada to Greenland occurred as recently as 140 years ago (14).

Health status of Canada's Aboriginal communities

Aboriginal communities in Canada have unfavourable profiles with respect to social and economic factors that strongly influence health (9,15). Consequently, on average, Aboriginal people die earlier and suffer a greater overall burden of disease than other Canadians (9). For example, in 2003, the life expectancy at birth among all Canadians, First Nations and Inuits was 76, 69 and 68 years, respectively, for men; and 82, 77 and 70 years, respectively, for women; infant mortality among First Nations and Inuit remained higher than the national average (9). The prevalence of particular chronic disease risk factors is elevated (15), notably smoking and obesity among both Inuit and First Nations, and diabetes among First Nations (9,16). However, injury and preventable infectious diseases represent strikingly disproportionate burdens, which is typical for nonaffluent populations with relatively young age distributions (9). In 2000, among causes of lost potential years of life, injury was more prevalent among First Nations than all other causes of death combined, and nearly 3.5 times as prevalent than among the total Canadian population (16). In the same year, First Nations communities had elevated rates, relative to Canada's average, of pertussis (2.2 times higher), rubella (seven times higher), tuberculosis (six times higher) and shigellosis (2.1 times higher) (16). First Nations hospitalization rates in 2000 were relatively high for all causes, except circulatory diseases and cancer; the rates were approximately two to three times higher than the Canadian average for injuries and poisonings, respiratory diseases and digestive diseases (16).

H pylori transmission

The *H pylori* mode of transmission remains uncertain; direct transmission from person to person is likely, but whether the pathway is primarily fecal-oral, oral-oral or gastric-oral (via regurgitated stomach contents) is debated (1,17). Compelling evidence suggests that *H pylori* may spread most readily through either vomiting or diarrhea during acute gastroenteritis caused by other agents (18). The existing evidence does not exclude the possibility of a contaminated environmental reservoir; findings were inconsistent from studies of domestic animals, drinking water and other reservoirs. Few attempts to culture *H pylori* from extragastric material were successful, but because of difficulties encountered in culturing this organism, the negative findings were not conclusive (1,17). *H pylori* has been detected in water, though usually by polymerase chain reaction, which does not indicate whether bacteria are viable (19); apparent isolation of viable *H pylori* from untreated wastewater in Mexico has been reported (20). Epidemiological reports tend to link poor drinking water quality with *H pylori* frequency, but the association is inconsistent in magnitude (19), perhaps due to diverse cultural practices across populations (1). In 2005, the US Geological Survey (21) reported polymerase chain reaction-based detection of *H pylori* in North American rivers, including the Yukon River and two tributaries in Alaska. *H pylori* concentrations were greater in riverbed sediment than in water, and were not associated with fecal contamination indicators. The levels of *H pylori* detected in the Alaskan rivers were considered too low to infect humans; however, the samples were collected from sparsely populated regions where the water quality was relatively pristine.

METHODS

A systematic search for literature on humans was conducted using six databases (PubMed; EMBASE; BIOSIS Previews; Native Health Research Database; Canadian Business & Current Affairs Reference; Arctic Science and Technology Information System), using the following search terms (Medical Subject Headings): *Helicobacter pylori*; *Helicobacter*

infections; Gastritis; Peptic ulcer; Dyspepsia; Anemia, Iron-Deficiency; Inuits; Indians, North American; Alaska; Nunavut; Northwest Territories; Yukon Territory; Arctic Regions; Canada; Greenland. This search yielded 296 papers, of which 69 were identified as relevant: 21 on topics related to *H pylori* in Canadian Aboriginals; 29 on topics related to *H pylori* in Alaska Natives; 12 on topics related to *H pylori* in Aboriginals of other Arctic regions (Greenland, Northern Europe, Eurasia); five reporting *H pylori* prevalence in Canadian populations not restricted to symptomatic patients; and two reporting *H pylori* prevalence in a large cross-Canada study of dyspeptic adults. Two additional references were pearled from the bibliographies of identified papers. The identified papers were organized by subtopic, and findings were summarized in narrative form. Key data from studies that reported *H pylori* prevalence for identified populations were summarized in tabular form. Because of the heterogeneous nature of the study populations represented in the literature, no quantitative summary measures were estimated.

RESULTS

The following subtopics were represented in the identified literature: *H pylori* infection in Canada; *H pylori* infection in northern Aboriginal populations; potential health effects of *H pylori* infection in northern Aboriginal populations; and effectiveness of *H pylori* therapy in northern Aboriginal populations.

H pylori infection in Canada

Eight studies that yielded *H pylori* prevalence estimates for Canadian populations (Table 1) were identified. There were no prevalence estimates for Canada overall, but the estimates from a random sample of Nova Scotia adults (22) are similar to those reported for a large representative survey of US adults (23); the Nova Scotia prevalence was 38% in all ages combined, increasing from 21% among 20- to 29-year-olds to 50% among 70- to 79-year-olds. Similarly, a study of Manitoba adults showed an *H pylori* prevalence of 35% (24). Recent cross-Canada studies revealed an *H pylori* prevalence of 30% in 1013 family practice patients with uninvestigated dyspepsia (25), and 5% in 246 pediatric patients from urban academic centres (4).

H pylori infection in northern Aboriginal populations

Studies of Aboriginal populations in the circumpolar region show elevated *H pylori* prevalence in Greenland, Russia, Alaska and Canada (Table 1). The *H pylori* prevalence in 71 indigenous Greenlanders, aged 22 to 76 years, randomly recruited for a population survey in the capital, Nuuk, between 1993 and 1994 was compared with that of 2794 Caucasian Danes, aged 30 to 60 years, who participated in a survey between 1983 and 1984 (26). Among the Greenlanders, 47% were seropositive for *H pylori* and 25% had borderline antibody levels, while among the Danes, 26% were seropositive and 19% had borderline antibody levels. In a population-based sample of 685 residents of Sisimiut (27), the second largest town in Greenland, the *H pylori* seroprevalence among those aged 15 to 87 years was 58%. Other studies of Greenland Natives show high *H pylori* prevalence in dyspeptic adults (28,29). Among 34 Chutkotka Natives, comprising 72% of the adult male population of a coastal Arctic settlement in Russia, *H pylori* infection was diagnosed histologically in 77% (30). Among 610 Alaska Natives from villages on Norton Sound, *H pylori* seropositivity was 80%; 72% were seropositive by 24 years of age (31). In Canada, reported *H pylori* seroprevalence was 51% among 256 Inuit in Nunavut (32), and 95% in 306 adult members of a First Nations community in northern Manitoba, where the prevalence by stool antigen test among 163 children aged 12 years and under was 56% (33,34). Another study compared *H pylori* seroprevalence in cord blood samples from 100 Inuit women giving birth in Nunavik, in northern Quebec, to samples from 99 women of unspecified ethnicity giving birth in southern Quebec; the seroprevalence was 27% in the northern women and 10% in the southern women (35).

Potential health effects of *H pylori* infection in northern Aboriginal populations

Reports of elevated prevalence of iron deficiency and anemia in Aboriginal Alaskans date back to the 1950s (36), with early recognition that the anemia could be from infection, because the prevalence of low serum transferrin saturation and anemia remained high following improvement of iron stores after supplementation (37). Renewed interest in iron deficiency and anemia in northern Aboriginals was reflected in the literature since 1988 for Alaska (38-42), and since 1998 for Canada (35,43-47), with continued recognition of the potential role of infection (40,46). The impact of changes in traditional diets has been examined as well (41,48,49).

Research on iron deficiency in Alaska Natives led Centers for Disease Control Arctic Investigations Program researchers and collaborators to link anemia with high *H pylori* prevalence in this population. In 1997, Yip et al (50) reported a high prevalence of iron deficiency among 140 Yupik adults from three villages in western Alaska; 90% had elevated fecal hemoglobin levels, 70 of whom underwent endoscopy; 68 (97%) had grossly abnormal gastric mucosa with erythema and mucosal thickening, 52 (74%) had diffuse intraepithelial hemorrhages, and 30 (43%) had gastric ulcers or multiple erosions; 68 of 69 (99%) examined for *H pylori* infection were infected. The Centers for Disease Control researchers examined 68% (688 children) of the seven- to 11-year-olds from 10 Alaska Native villages in southwestern Alaska, and reported that 86% were *H pylori*-positive by urea breath test, 38% had iron deficiency and 8% had anemia; *H pylori* infection was associated with both iron deficiency and anemia (51). A subsequent treatment trial (52) showed, however, that neither iron deficiency nor mild anemia clearly improved in successfully treated children (as demonstrated by urea breath test negativity) at two, eight or 14 months after treatment, although a study in younger Bangladeshi children (53) showed that the presence of *H pylori* infection was associated with a reduced response to iron supplementation. In the Alaskan trial (54), children who remained infected were not observed to experience decreased growth during this age period, although such effects have been reported for younger children in Andean South America (55,56). Among 115 children aged four to 18 months from one Inuit and two Cree communities in Nunavut and northern Ontario, 36% with anemia and 53% with low iron stores, *H pylori* seropositivity was associated with anemia, but associations weakened substantially after controlling for dietary factors (57). In this young age group, however, *H pylori*-infected children can be antibody-negative, and seropositivity in infants may largely reflect maternal antibodies (58).

With respect to diseases known to result from *H pylori* infection, increased occurrence of gastric ulcer relative to duodenal ulcers was reported for Greenlanders (59), residents of Arctic Norway (60), Alaska Natives (50,61) and the Inuit of northern Labrador (62). Age-adjusted comparisons from province-wide data for Manitoba from 1989 to 1993 (33) showed that Registered Indians had nearly twice the rate of hospitalizations associated with peptic ulcer disease diagnoses compared with persons not registered with the federal government as Indian, and gastric cancer incidence rates were similar in the two groups. While statistics on peptic ulcer disease frequency are not routinely accessible for population subgroups, cancer statistics specific to Aboriginal populations are available for some geographic regions. Reported data from the US National Cancer Institute Surveillance Epidemiology and End Results Program for 1988 to 1992 (63) showed that stomach cancer incidence rates in Alaska Native men were nearly three times the rate in American non-Hispanic white men. Reported 1990 to 2000 data on cancer frequency in the Canadian Northwest Territories (64), where one-half of the population is Aboriginal, show that stomach cancer was the fourth most frequently diagnosed cancer in Northwest Territories men, in contrast to 10th for men across Canada; in Dene (Athabascan First Nations) men, stomach cancer was tied for third place with prostate cancer, each accounting for 7% cancers diagnosed, while among Inuit men, stomach cancer was second after lung cancer, accounting for 16% of cancers diagnosed. Increased proportional incidence for cancer subtypes may not reflect increased incidence rates if the overall frequency of cancer is lower; compared with the all-cancer incidence rate in men across Canada, the age-adjusted rates for Northwest Territories men were similar in Inuit, 15% lower in Métis and 20% lower in Dene populations. Adjusting for age, the stomach cancer incidence rate in all Northwest Territories men is nearly twice the rate in Canadian men, and nearly threefold for outlying regional centres where the population is predominantly Aboriginal (Inuvik, Hay River, Fort Smith). Northwest Territories cancer mortality rates (1990 to 1999) showed that stomach cancer was the third most frequent cause of cancer mortality, at 6% of cancer deaths in men, compared with ninth for men across Canada; among Dene men, stomach cancer accounted for 10% of cancer deaths. Stomach cancer resulted in 7% of potential years of life lost due to cancer for both men and women in the Northwest Territories (1990 to 1999), compared with 2.7% for men and 2.2% for women across Canada (64,65).

Effectiveness of *H pylori* therapy in northern Aboriginal populations

Published reports on the effectiveness of antibiotic treatment aimed at eliminating *H pylori* infection in northern Aboriginals are limited to three studies conducted in Alaska. Among 125 adult Alaska Native patients in Anchorage, 30% of *H pylori* isolates were resistant to clarithromycin and 66% to metronidazole (66); resistance to clarithromycin or metronidazole was associated with use of any macrolide antibiotic or metronidazole, respectively, during the preceding eight to 10 years. Among 96 patients who had a urea breath test eight weeks after treatment, 71% tested negative. Among those treated with clarithromycin-based regimens, treatment failed in 77% of those with clarithromycin-resistant strains and 13% of those with clarithromycin-susceptible strains, while metronidazole resistance did not appear to be associated with treatment failure. In another study (67), 98 successfully treated Anchorage adults (negative breath test eight weeks after therapy) were followed to estimate the frequency of reinfection, defined by a positive breath test; the reinfection rate was 7% at six months, 10% at one year, and 15% at two years, which was higher than reinfection rates typically observed in settings with modern sanitation infrastructure, generally under 5% per year (68,69). In a randomized treatment trial (70), 219 *H pylori*-infected, iron-deficient children identified in the study of rural Alaskan seven- to 11-year-olds were treated with either iron sulfate alone or in combination with a two-week course of lanzoprazole, clarithromycin and amoxicillin; those allergic to amoxicillin or macrolides received metronidazole. Two months after initial therapy, only 34% of the antibiotic group (and 1% of the iron-only group) had a negative breath test. Factors associated with treatment success included metronidazole treatment, complete dosage, fewer household members and higher body mass index. Among 50 children who failed initial therapy and were retreated with two weeks of metronidazole-based quadruple therapy, 84% tested *H pylori*-negative eight months later.

Canadian data on antibiotic resistance were summarized in a systematic review (71), published in 2000, on *H pylori* resistance to clarithromycin or metronidazole. Among studies that excluded previously treated patients, estimates of resistance ranged from 18% to 22% for metronidazole, and less than 4% for clarithromycin. Resistance frequencies were higher on average in studies that included previously treated patients. Information specific to Aboriginal populations was not available.

CONCLUSIONS

Consistent with its association with premodern or impoverished living conditions, *H pylori* infection is highly prevalent among northern Aboriginal populations. Although data on disease rates for these groups come from small studies, evidence suggests that *H pylori*-associated digestive diseases are important health problems in northern Aboriginal communities, and that antibiotic resistance and other factors may contribute to high rates of treatment failure. In addition, some reports link the high prevalence of anemia in these populations to *H pylori* infection, although the existing evidence does not clearly support a cause-effect relation (72). Few community-based studies of *H pylori* infection have been conducted in Canada. Although evidence from Alaska provides information from related Inuit communities, it cannot be assumed that all of the Alaskan findings apply to Inuit communities in Canada or other countries, given differences in access to health care and other resources. Similarly, the data reported for a small number of Canadian Aboriginal populations cannot be assumed to apply across Canada. In the Northwest Territories, health officials recognized the need to address community concerns about health risks from *H pylori* infection (Andre Corriveau, Chief Medical Health Officer, and John Morse, Medical Directors' Forum Chair, personal communication), but lack information regarding the extent of the problem or cost-effective solutions. Local population-based research is needed to assess the disease burden that is attributable to *H pylori* infection and arrive at public health policies that protect community health.

There is sufficient evidence, however, to include Canadian and other Arctic Aboriginal populations among ethnic groups

at increased risk of *H pylori* infection and its consequences, including gastric cancer, and among those at increased risk of treatment failure. The American Society for Gastrointestinal Endoscopy guidelines (73) include ethnic background associated with increased risk of upper gastrointestinal malignancies or other significant disease states as a high-risk indicator among dyspeptic patients, and consequently, an indication for the use of endoscopy to investigate dyspepsia. Furthermore, the current Canadian Helicobacter Study Group Consensus (74) recommends that individuals from an ethnic or geographic background associated with a high risk of gastric cancer should be considered for a 'search and treat' strategy for *H pylori* infection. Based on the evidence, it would be warranted for clinicians to relax the criteria for investigating *H pylori* and related diseases in patients from Arctic Aboriginal communities, and to pursue post-therapy confirmation of eradication.

REFERENCES

1. Goodman KJ, Correa P. The transmission of *Helicobacter pylori*. A critical review of the evidence. Int J Epidemiol 1995;24:875-87.
2. The Nobel Prize in Physiology or Medicine 2005. <http://nobelprize.org/nobel_prizes/medicine/laureates/2005/press.html> (Version current at February 19, 2008).
3. CANCERMondial. Globocan 2002. <http://www-dep.iarc.fr> (Version current at February 19, 2008).
4. Jacobson K. The changing prevalence of *Helicobacter pylori* infection in Canadian children: Should screening be performed in high-risk children? Can J Gastroenterol 2005;19:412-4.
5. 2001 Census: Analysis series. Aboriginal peoples of Canada: A demographic profile. <http://www12.statcan.ca/english/census01/products/analytic/companion/abor/pdf/96F0030XIE2001007.pdf> (Version current at February 19, 2008).
6. First Nation Information Project. <http://www.aboriginalcanada.com/firstnation/dirfnatl.htm> (Version current at February 19, 2007).
7. Métis National Council. Who are the Métis? <http://www.metisnation.ca/who/index.html> (Version current at February 19, 2008).
8. Inuit Tapiriit Kanatami. Our 5000 year heritage. <http://www.itk.ca/5000-year-heritage> (Version current at February 19, 2008).
9. Aboriginal Peoples' Health. In: Canadian Population Health Initiative. Improving the Health of Canadians. Ottawa: Canadian Institute for Health Information, 2004:86-116.
10. Greenland in Figures 2007. <http://www.statgreen.gl/dk/aarbog/Greenland%20in%20figures%202007.pdf> (Version current at February 19, 2008).
11. US Census Bureau. State & County QuickFacts. Alaska. <http://quickfacts.census.gov/qfd/states/02000.html> (Version current at February 19, 2008).
12. Alaska Native Heritage Center. <http://www.alaskanative.net> (Version current at February 19, 2008).
13. Inuvialuit. <http://en.wikipedia.org/wiki/Inuvialuit> (Version current at February 19, 2008).
14. Greenland Guide. Culture & History. <http://www.greenland-guide.gl/culture_history.htm> (Version current at February 19, 2008).
15. Tjepkema M. The health of the off-reserve Aboriginal population. Statistics Canada. Health Reports 2002;13(Suppl):73-88.
16. Statistical profile on the health of First Nations in Canada. <http://www.hc-sc.gc.ca/fnih-spni/pubs/gen/stats_profil_e.html> (Version current at February 19, 2008).
17. Brown LM. *Helicobacter pylori*: Epidemiology and routes of transmission. Epidemiol Rev 2000;22:283-97.
18. Parsonnet J, Shmuely H, Haggerty T. Fecal and oral shedding of *Helicobacter pylori* from healthy infected adults. JAMA 1999;282:2240-5.
19. Travis PB. Association of water quality and sewage disposal with *Helicobacter pylori* incidence in infants. PhD dissertation, Medical University of South Carolina, 2007.
20. Lu Y, Redlinger TE, Avitia R, Galindo A, Goodman K. Isolation and genotyping of *Helicobacter pylori* from untreated municipal wastewater. Appl Environ Microbiol 2002;68:1436-9.
21. Voytek MA, Ashen JB, Fogarty LR, Kirshtein JD, Landa ER. Detection of *Helicobacter pylori* and fecal indicator bacteria in five North American rivers. J Water Health 2005;3:405-22.
22. Veldhuyzen van Zanten SJ, Pollak PT, Best LM, Bezanson GS, Marrie T. Increasing prevalence of *Helicobacter pylori* infection with age: Continuous risk of infection in adults rather than cohort effect. J Infect Dis 1994;169:434-7.
23. Everhart JE, Kruszon-Moran D, Perez-Perez GI, Tralka TS, McQuillan G. Seroprevalence and ethnic differences in *Helicobacter pylori* infection among adults in the United States. J Infect Dis 2000;181:1359-63.
24. Pérez-Pérez GI, Bhat N, Gaensbauer J, et al. Country-specific constancy by age in cagA+ proportion of *Helicobacter pylori* infections. Int J Cancer 1997;72:453-6.
25. Thomson AB, Barkun AN, Armstrong D, et al. The prevalence of clinically significant endoscopic findings in primary care patients with uninvestigated dyspepsia: The Canadian Adult Dyspepsia Empiric Treatment – Prompt Endoscopy (CADET-PE) study. Aliment Pharmacol Ther 2003;17:1481-91.
26. Milman N, Byg KE, Andersen LP, Mulvad G, Pedersen HS, Bjerregaard P. Indigenous Greenlanders have a higher seroprevalence of IgG antibodies to *Helicobacter pylori* than Danes. Int J Circumpolar Health 2003;62:54-60.
27. Koch A, Krause TG, Krogfelt K, Olsen OR, Fischer TK, Melbye M. Seroprevalence and risk factors for *Helicobacter pylori* infection in Greenlanders. Helicobacter 2005;10:433-42.
28. Fenger HJ, Gudmand-Høyer E. Peptic ulcer in Greenland Inuit: Evidence for a low prevalence of duodenal ulcer. Int J Circumpolar Health 1997;56:64-9.
29. Johansen JK, Sehested A, Myrhøj T, Ladefoged K, Krogfelt KA. *Helicobacter pylori* infection in Greenlandic patients with dyspepsia. Int J Circumpolar Health 2004;63(Suppl 2):219-20.
30. Reshetnikov OV, Nikitin YP, Kholmogortsev MV, Kurilovich SA, Pycllik OA. *Helicobacter pylori* in a Chukotka Native male population. Int J Circumpolar Health 1998;57(Suppl 1):293-5.
31. Zhu J, Davidson M, Leinonen M, et al. Prevalence and persistence of antibodies to herpes viruses, *Chlamydia pneumoniae* and *Helicobacter pylori* in Alaskan Eskimos: The GOCADAN Study. Clin Microbiol Infect 2006;12:118-22.
32. McKeown I, Orr P, Macdonald S, et al. *Helicobacter pylori* in the Canadian arctic: Seroprevalence and detection in community water samples. Am J Gastroenterol 1999;94:1823-9.
33. Bernstein CN, McKeown I, Embil JM, et al. Seroprevalence of *Helicobacter pylori*, incidence of gastric cancer, and peptic ulcer-associated hospitalizations in a Canadian Indian population. Dig Dis Sci 1999;44:668-74.
34. Sinha SK, Martin B, Sargent M, McConnell JP, Bernstein CN. Age at acquisition of *Helicobacter pylori* in a pediatric Canadian First Nations population. Helicobacter 2002;7:76-85.
35. Hodgins S, Dewailly E, Chatwood S, Bruneau S, Bernier F. Iron-deficiency anemia in Nunavik: Pregnancy and infancy. Int J Circumpolar Health 1998;57(Suppl 1):135-40.
36. Butler JC, Parkinson AJ, Funk E, Beller M, Hayes G, Hughes JM. Emerging infectious diseases in Alaska and the Arctic: A review and a strategy for the 21st century. Alaska Med 1999;41:35-43.
37. Burks JM, Siimes MA, Mentzer WC, Dallman PR. Iron deficiency in an Eskimo village. The value of serum ferritin in assessing iron nutrition before and after a three-month period of iron supplementation. J Pediatr 1976;88:224-8.
38. Centers for Disease Control (CDC). High prevalence of iron deficiency anemia among Alaskan native children. MMWR Morb Mortal Wkly Rep 1988;37:200-2.
39. Leads from the MMWR. High prevalence of iron deficiency anemia among Alaskan Native children. JAMA 1988;259:2532.
40. Cruz A, Parkinson AJ, Hall D, Bulkow L, Heyward W. Associations of early childhood infections and reduced hemoglobin levels in a

historic cohort of Alaska Native infants. Arctic Med Res 1990;49:175-9.
41. Nobmann ED, Byers T, Lanier AP, Hankin JH, Jackson MY. The diet of Alaska Native adults: 1987-1988. Am J Clin Nutr 1992;55:1024-32.
42. Petersen KM, Parkinson AJ, Nobmann ED, Bulkow L, Yip R, Mokdad A. Iron deficiency anemia among Alaska Natives may be due to fecal loss rather than inadequate intake. J Nutr 1996;126:2774-83.
43. Willows ND, Dewailly E, Gray-Donald K. Anemia and iron status in Inuit infants from northern Quebec. Can J Public Health 2000;91:407-10.
44. Willows ND, Morel J, Gray-Donald K. Prevalence of anemia among James Bay Cree infants of northern Quebec. CMAJ 2000;162:323-6.
45. Willows ND, Gray-Donald K. Blood lead concentrations and iron deficiency in Canadian aboriginal infants. Sci Total Environ 2002;289:255-60.
46. Willows ND, Gray-Donald K. Infection and anemia in Canadian aboriginal infants. Can J Diet Pract Res 2004;65:180-2.
47. Christofides A, Schauer C, Sharieff W, Zlotkin SH. Acceptability of micronutrient sprinkles: A new food-based approach for delivering iron to First Nations and Inuit children in Northern Canada. Chronic Dis Can 2005;26:114-20.
48. Milman N, Byg KE, Mulvad G, Pedersen HS, Bjerregaard P. Iron status markers in 224 indigenous Greenlanders: Influence of age, residence and traditional foods. Eur J Haematol 2001;66:115-25.
49. Kozlov A. Impact of economic changes on the diet of Chukotka Natives. Int J Circumpolar Health 2004;63:235-42.
50. Yip R, Limburg PJ, Ahlquist DA, et al. Pervasive occult gastrointestinal bleeding in an Alaska native population with prevalent iron deficiency. Role of *Helicobacter pylori* gastritis. JAMA 1997;277:1135-9.
51. Baggett HC, Parkinson AJ, Muth PT, Gold BD, Gessner BD. Endemic iron deficiency associated with *Helicobacter pylori* infection among school-aged children in Alaska. Pediatrics 2006;117:e396-404.
52. Gessner BD, Baggett HC, Muth PT, et al. A controlled, household-randomized, open-label trial of the effect that treatment of *Helicobacter pylori* infection has on iron deficiency in children in rural Alaska. J Infect Dis 2006;193:537-46.
53. Mahalanabis D, Islam MA, Shaikh S, et al. Haematological response to iron supplementation is reduced in children with asymptomatic *Helicobacter pylori* infection. Br J Nutr 2005;94:969-75.
54. Chimonas MA, Baggett HC, Parkinson AJ, Muth PT, Dunaway E, Gessner BD. Asymptomatic *Helicobacter pylori* infection and iron deficiency are not associated with decreased growth among Alaska Native children aged 7-11 years. Helicobacter 2006;11:159-67.
55. Bravo LE, Mera R, Reina JC, et al. Impact of *Helicobacter pylori* infection on growth of children: A prospective cohort study. J Pediatr Gastroenterol Nutr 2003;37:614-9.
56. Passaro DJ, Taylor DN, Gilman RH, Cabrera L, Parsonnet J. Growth slowing after acute *Helicobacter pylori* infection is age-dependent. J Pediatr Gastroenterol Nutr 2002;35:522-6.
57. Christofides A, Schauer C, Zlotkin SH. Iron deficiency and anemia prevalence and associated etiologic risk factors in First Nations and Inuit communities in Northern Ontario and Nunavut. Can J Public Health 2005;96:304-7.
58. Goodman KJ, Cockburn M. The role of epidemiology in understanding the health effects of *Helicobacter pylori*. Epidemiology 2001;12:266-71.
59. Ingeman-Nielsen MW. [Radiographic examination of the stomach in Greenlanders]. Ugeskr Laeger 1990;152:2646-9.
60. Eriksen BO, Garpestad OK, Søndenå H, Burhol PG. Peptic ulcer patterns in Arctic Norway. J Clin Gastroenterol 1995;20:100-3.
61. Thompson WM, Ackerstein H. Peptic ulcer disease in the Alaska natives: A four-year retrospective study. Alaska Med 1975;17:43-4.
62. William G, Fitzgerald N, Ehrenkranz RL. The seasonal occurrence of peptic ulcer disease among the Inuit of northern Labrador. In: Fortuine R, ed. Circumpolar Health 84: Proceedings of the Sixth International Symposium on Circumpolar Health Seattle: University of Washington Press, 1985:285-7.
63. Miller BA, Kolonel LN, Bernstein L, et al (eds). Racial/Ethnic Patterns of Cancer in the United States 1988-1992. Bethesda: National Cancer Institute, 1996.
64. Cancer in the Northwest Territories 1990-2000. A descriptive report. <http://www.hlthss.gov.nt.ca/pdf/reports/diseases_and_conditions/2003/english/cancer_in_the_nwt.pdf> (Version current at February 19, 2008).
65. Canadian Cancer Statistics 2006. <http://www.cancer.ca/vgn/images/portal/cit_86751114/31/21/935505792cw_2006stats_en.pdf.pdf> (Version current at February 19, 2008).
66. McMahon BJ, Hennessy TW, Bensler JM, et al. The relationship among previous antimicrobial use, antimicrobial resistance, and treatment outcomes for *Helicobacter pylori* infections. Ann Intern Med 2003;139:463-9.
67. McMahon BJ, Bruce MG, Hennessy TW, et al. Reinfection after successful eradication of *Helicobacter pylori*: A 2-year prospective study in Alaska Natives. Aliment Pharmacol Ther 2006;23:1215-23.
68. Xia HX, Talley NJ, Keane CT, O'Morain CA. Recurrence of *Helicobacter pylori* infection after successful eradication: Nature and possible causes. Dig Dis Sci 1997;42:1821-34.
69. Parsonnet J. What is the *Helicobacter pylori* global reinfection rate? Can J Gastroenterol 2003;17(Suppl B):46B-8B.
70. Gessner BD, Bruce MG, Parkinson AJ, et al. A randomized trial of triple therapy for pediatric *Helicobacter pylori* infection and risk factors for treatment failure in a population with a high prevalence of infection. Clin Infect Dis 2005;41:1261-8.
71. Fallone CA. Epidemiology of the antibiotic resistance of *Helicobacter pylori* in Canada. Can J Gastroenterol 2000;14:879-82.
72. Goodman KJ, Joyce SL, Ismond KP. Extragastric diseases associated with *Helicobacter pylori* infection. Curr Gastroenterol Rep 2006;8:458-64.
73. Eisen GM, Dominitz JA, Faigel DO, et al. The role of endoscopy in dyspepsia. Gastrointest Endosc 2001;54:815-7.
74. Hunt R, Fallone C, van Zanten SV, et al. Canadian Helicobacter Study Group Consensus Conference: Update on the management of *Helicobacter pylori* – An evidence-based evaluation of six topics relevant to clinical outcomes in patients evaluated for *H pylori* infection. Can J Gastroenterol 2004;18:547-54.
75. Drumm B, Perez-Perez GI, Blaser MJ, Sherman PM. Intrafamilial clustering of *Helicobacter pylori* infection. N Engl J Med 1990;322:359-63.
76. Armstrong D, Veldhuyzen van Zanten SJ, Barkun AN, et al. Heartburn-dominant, uninvestigated dyspepsia: A comparison of 'PPI-start' and 'H2-RA-start' management strategies in primary care – the CADET-HR Study. Aliment Pharmacol Ther 2005;21:1189-202.